Pharmacokinetics of a multipurpose pod-intravaginal ring simultaneously delivering five drugs in the ovine model

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Supplemental Material

MATERIALS AND METHODS

Bioanalysis methods. Samples were prepared for bioanalysis by filtration (CVL) or protein precipitation (plasma, pulverized tissue) and were analyzed by LC-MS using an Agilent Series 1100 LC coupled to an Agilent 1100 single-quadrupole MSD and ESI source with instrument control and data analysis using ChemStation software. The LC-MS methods were as follows:

TFV, NVP, SQV, and ETG in CVL: naproxen internal standard; Zorbax Eclipse XDB-C8 column (2.1 × 150 mm 3.5 μm, Agilent); gradient program: 3 min hold at 100:0 A:B (A, 0.1% acetic acid in water; B, 0.1% acetic acid in methanol), 22 min ramp to 27:73 A:B; ESI^+ detection.

TFV, NVP, SQV, and ETG in vaginal tissues: naproxen internal standard; Zorbax Poroshell 300SB-C3 column (2.1 × 150 mm 5 μm, Agilent); gradient program: 3 min hold at 100: 0 A:B (A, 0.1% acetic acid in water; B, 0.1% acetic acid in methanol), 27 min ramp to 0:100 A:B; ESI^+ detection.

EE in CVL and vaginal tissue: naproxen internal standard; ODS Hypersil column (2.1 × 150 mm 3 μm, Agilent); gradient program: 4 min ramp from 90:10 A:B (A, 15 mM ammonium hydroxide in water; B, acetonitrile), 5 min ramp from 50:50 to 0:100 A:B (for vaginal tissues, 4 min ramp from 90:10 A:B to 0:100 A:B, 1 min hold at A:B 0:100); ESI^- detection.

For CVL, the LLOQs were: TFV, 5 ng mL^{-1}; NVP, 2.5 ng mL^{-1}; SQV, 5 ng mL^{-1}; ETG, 10 ng mL^{-1}; and EE, 0.5 ng mL^{-1}.

For tissue, the LLOQs were: TFV, 0.5 ng g^{-1}; NVP, 1 ng g^{-1}; SQV, 5 ng g^{-1}; ETG, 1 ng g^{-1}; and EE, 0.5 ng g^{-1}.